NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Heparin Induced Thrombocytopenia, Diagnosis and Treatment

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

NHS GG&C Clinical Haematology HIT Guideline

1. WHAT IS HIT?: Heparin–Induced Thrombocytopenia

An immune mediated adverse effect of heparin resulting in the development of an IgG antibody against the heparin/platelet factor 4 complex. This leads to platelet activation resulting in thrombocytopenia but can also paradoxically cause potentially fatal arterial and venous thromboses.

2. PREVENTION & MONITORING

HIT is a relatively rare but certain factors will increase the risk of it developing. It is important to identify these high risk groups early to ensure the platelet count is sufficiently monitored.

1. **Patient group:** Surgical > Medical > Obstetric patients
2. **Type of heparin:** Unfractionated heparin (UFH) > Low molecular weight heparin (LMWH)
3. **Dose of heparin:** Treatment dose > Prophylactic dose > Line flush

All Patients	Baseline platelet count on the day of starting heparin.
All post-operative patients on UFH (and post cardio-pulmonary bypass (CPB) patients on LMWH)	Platelet counts on alternate days from days 4-14 or until stopped.
Obstetric and Medical patients on LMWH	No need for routine monitoring.
Post-op patients (except post-CPB patients) on LMWH	No need for routine monitoring.
2^{nd} exposure to Heparin within 100 days	Baseline count & further count 24 hours after commencing heparin.

3. DIAGNOSIS

HIT is a difficult condition to diagnose – it is relatively rare and patients often have other possible causes of thrombocytopenia to which the condition is attributed. The diagnosis of HIT is primarily clinical. The presentation can be variable but is most often asymptomatic thrombocytopenia. Local skin reactions, skin necrosis and acute systemic reactions can sometimes be presenting features. Spontaneous haemorrhage and petechiae do not tend to occur. Two important factors to consider are:

1. **Timing of onset of thrombocytopenia in relation to starting heparin.**

Thrombocytopenia tends to occur after 5-10 days of exposure to heparin. This is the time taken for HIT antibodies to be formed. If a patient has been exposed to heparin within the past 100 days then thrombocytopenia can occur within 24 hours as a result of preformed antibodies.

2. **Extent of thrombocytopenia.**

The platelet count tends to drop quite suddenly by a factor of 30-50%. It is rare for the platelet count to fall to less than 20×10^9/l.

The likelihood of a patient having HIT can be predicted on the basis of the following clinical scoring system thought of as “the four Ts of HIT.”

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"The Four Ts"	Points (0, 1, 2 for each of 4 categories; maximum score = 8)		
	2 points	1 point	0 points
Timing	Onset between d5-10; or ≤ 1 day if 2nd exposure within 30 days	Onset after d10; or ≤ 1 day if 2nd exposure within 30-100 days; or time of onset unclear	Onset ≤ d4 without recent Heparin exposure
Thrombocytopenia	>50% fall and Platelet nadir ≥ $20x10^9$/l	30-50% fall or Platelet nadir $10\text{-}19x10^9$/l	<30% fall or Platelet nadir < $10x10^9$/l
Thrombosis	New thrombosis; Skin necrosis; Acute systemic reaction	Suspected thrombosis – not yet confirmed; Progressive or recurrent thrombosis; Erythematous lesions	None
o**T**her causes of thrombocytopenia e.g. drugs (see BNF), sepsis, DIC, BM failure etc.	No other cause evident	Possible other cause identifiable	Definite other cause is present

6-8 points = high risk of HIT; 4-5 points = intermediate risk; 0-3 points = low risk

If the score is **low** – HIT would be very unlikely and there is **no need for investigation**.
It is advised to repeat the score again on subsequent days to ensure the risk has not increased.

Patients who fall into the **high** or **intermediate** risk groups should be treated as though they have HIT until proven otherwise.

INVESTIGATIONS:
Samples required: 3.5 ml Sodium Citrate (blue top) sent to Haematology. HIT assays can be requested on Trakcare, or by using the specific HIT assay request form which can be downloaded from Staffnet.

Heparin-Induced Thrombocytopenia (HIT) Antibody Assay Request (hyperlink when available)

The Specialist Haemostasis Laboratory at Glasgow Royal Infirmary currently uses an assay on the ACL AcuStar (Instrumentation Laboratory) for the analysis of HIT IgG antibodies. The AcuStar method is performed on an automated platform, using chemiluminescent technology. The AcuStar assay shows good agreement when compared with the PaGIA rapid gel test and the HIT IgG ELISA assay previously offered by SNBTS.

Results equal or higher than 1U/mL may indicate the presence of HIT antibodies.

4. MANAGEMENT OF HIT

STOP heparin and immediately replace with a therapeutic dose of an alternative anticoagulant, even whilst the platelet count is still low.
Treat for at least 48 hours and until platelet count has recovered – (highest risk period for thrombosis is after stopping heparin).
AVOID platelet transfusions if possible – patients very rarely bleed.

1st choice: Danaparoid – if tolerant or renal impairment [CrCl <30ml/min], consider 2nd choice
2nd choice: Argatroban – contraindicated in severe hepatic impairment [Child-Pugh Class C, or liver failure]

Dosing	IV Bolus	IV Infusion	Monitoring (Target range)
Danaparoid	<55kg: 1250 units 55-90kg: 2500 units >90kg: 3750 units	400 units/h for 2h, then 300 units/h for 2h, then 200 units/h thereafter	Only required in renal impairment [CrCl <30ml/min] or weight >90kg. Target anti-Xa level 0.5-0.8 units/ml
Argatroban Standard dose	None	Start at 2 microgram/kg per min Using a 1mg/ml solution	APTT ratio 1.5 – 3.0* Repeat within of 2h of dose change and at least daily
Argatroban Critically ill, post-cardiac surgery, or moderate liver disease [Child-Pugh Class B]	None	Start at 0.5 microgram/kg per min	APTT ratio 1.5 – 3.0* Repeat within of 4h of dose change and at least daily

*If APTT ratio exceeds 3.0 stop Argartoban infusion for 2h until APTT ratio falls to <3.0 and infusion can be restarted at a lower dose.

Transition to oral anticoagulation [this should be discussed with a haematologist]

Warfarin
Warfarin should not be commenced until the platelet count has normalised (or the patient's pre-heparin baseline platelet count has been reached) and at least 5-7 days have elapsed since the heparin has been discontinued.
During warfarin loading until INR is therapeutic, and for at least a 5 day overlap, therapeutic anticoagulation should be maintained with non-heparin anticoagulant (e.g. continuous IV infusion of Danaparoid or Argartroban [or in cardiac patients, Bivalirudin may be suitable alternative]; or possibly daily subcutaneous Fondaparinux).
Transition from Argatroban to warfarin is complicated because Argatroban will increase the PT and INR making determination of achievement of therapeutic warfarin difficult – see suggested transition algorithm below. For this reason transition to one of the direct acting oral anticoagulant (e.g. Apixaban or Rivaroxaban) may be the preferred option in patients with venous thrombosis.

Alternatively, Fondaparinux may be used under the direction of a consultant haematologist to assist in the transition between Argatroban and oral anticoagulation with warfarin. Dosing is weight-based and clearance is predominantly renal, such that its use is contraindicated if CrCl <30ml/min.

Apixaban and Rivaroxaban

If the patient has suffered venous thrombosis, then 3-6 months oral Apixaban or Rivaroxaban may be a preferable alternative to warfarin. If the patient is suitable for either of these agents, this can be commenced when the platelet count has normalised (or the patient's pre-heparin baseline count has been reached) and at least 5-7 days have elapsed since the heparin has been discontinued. The parenteral anticoagulant (i.e. Danaparoid or Argatroban) should be discontinued when the first dose of Apixaban or Rivaroxaban is administered. Please see NHS GG&C guidance on the use of Apixaban or Rivaroxaban for the treatment of VTE, for dosing advice, duration and discharge information.

Duration of anticoagulation

- Patient should be therapeutically anticoagulated for at least 3 months after HIT with a thrombotic complication and for 4 weeks following HIT without a thrombotic complication.

Complicated cases

- Patients with possible diagnosis of HIT requiring surgery or haemodialysis – seek advice from Pharmacy/Haematology Department.

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Loading with warfarin after Argatroban

Argatroban increases the PT making assessment of the warfarin effect difficult. The following algorithm is recommended for determining when therapeutic warfarinisation has been achieved and Argatroban can be discontinued.